REMARKS

Claims 1-43 are pending in the present Application. Claims 5-7 and 11-43 have been withdrawn from consideration. Claims 1 and 8 have been amended, claims 2, 3, 9 and 10 have been cancelled, and claims 44 and 45 have been added, leaving Claims 1, 4, 8, 44 and 45 for consideration upon entry of the present Amendment.

Amendments to the Claims

Claims 1 and 8 have been amended to comprise a change in SEQ ID No. 1 from GAG to AAG at codon 50, corresponding to a G to A change at position 458. Support for this amendment can at least be found in Claims 3 and 10, respectively, as well as in Table 1 and Paragraph [020] as originally filed. Support for the addition of "continuous" can be found in the specification as filed at least in paragraph [037].

Claim 8 has also been amended to include the phrase "used detect or sequence optineurin polynucleotides by hybridization." Support for this amendment can be found at least in Paragraphs [050]-[055] as originally filed.

Support for new claims 44 and 45 can be found in claims 1-2 and 8-10 as filed, and in the specification in paragraph 37.

No new matter has been introduced by these amendments. Reconsideration and allowance of the claims are respectfully requested in view of the above amendments and the following remarks.

Amendments to the Specification

Support for the amendment to page 6, paragraph 14 can be found in the Specification as originally filed.

The amendment to insert the paragraphs after page 6, paragraph 14, submitted on 5/24/2004 has been amended according to the Examiner's suggestions. In particular, sentences 1-2, and 7-8 remain as filed. Sentences 3-6 have been deleted. No new matter has been introduced by these amendments.

The Examiner has also indicated that the Specification does not support the amendment filed on 5/24/2004 at page 28, paragraph 75. Accordingly, Applicants have cancelled the amendment to page 28, paragraph [075] filed on 5/24/2004 herein.

Elections/Restrictions

The Examiner has recognized that SEQ ID Nos. 1, 3, and 5 encode different isoforms of the same protein and are therefore not distinct and independent inventions. (Office Action dated 8/14/2006, page 1) Thus, SEQ ID Nos. 1, 3, and 5 are subject to an election of species rather than a restriction. Accordingly, Applicants have elected SEQ ID No. 1 for prosecution on the merits.

The Examiner also acknowledged the election with traverse to prosecute a change from GAG to AAG at codon 50 for claims 3 and 10. (Office Action dated 8/14/2006, page 3) The Examiner considered, but rejected, the argument that all of the mutations listed in claims 3 and 10 are mutations in the optineurin gene, and would not present an undue burden to search each mutation. (Office Action dated 8/14/2006, page 3) The Examiner found that searching each mutation would present a burden and that the restriction requirement was proper. As amended, Claims 1 and 8 are directed to an isolated nucleic acid comprising SEQ ID Nos. 1, "wherein the nucleic acid molecule comprises a change form GAG to AAG at codon 50, corresponding to a G to A change at position 458". Claims 3 and 10 have been cancelled accordingly.

Priority

Claims 1-4 have been awarded the priority benefit of the filing date of February 28, 2002, corresponding to the filing date of U.S. Serial No. 10/090,118. (Office Action dated 8/14/2006, pages 3-4) In particular, the Examiner refers to the sequence SEQ ID NO:1 and GenBank Accession # AF420371 referred to in U.S. Serial No. 10/090,118. Applicants note that the gene now called optineurin was available in the open literature, for example, as tumor necrosis factor-α (TNF-α) inducible protein (Li, Y. *et al., Mol. Cell. Biol. 18*:1601 (1998)), FIP-2 (for adenovirus E3-14.7K interacting protein 2), Huntingtin interacting protein L (HYPL) (Faber, P.W. *et al., Hum. Mol. Genet. 7*:1463 (1998)), NEMO-related protein (NRP) (Schwamborn, K. *et al., J. Biol. Chem. 275*:22780 (2000)), transcription factor IIIA interacting protein (TFIIIA-INTP) (Moreland,

R.J. *et al., Nucleic Acids Res.* 28:1986 (2000)), and RAB8-interacting protein (Hattula, K. and Peranen, J., *Curr. Bio. 10*:1603 (2000)). Thus, there were many sequences of the optineurin gene available at the time of filing date of U.S. Provisional Application No.: 60/344,754, filed on December 24, 2001.

Claims 8-10 have not been awarded benefit of any priority applications and have been given a filing date of 2/26/2003. (Office Action dated 8/14/2006, page 4) The Examiner contends that the priority applications do not appear to provide support for an array of nucleic acid molecules.

Information Disclosure Statement

Applicants note that the Examiner has not considered the art submitted in the Information Disclosure Statement dated November 3, 2006. Applicants respectfully request that the art submitted in this Information Disclosure Statement be considered and a fully initialed PTO Form A820 be returned to the Applicants.

Specification

The Examiner has objected to the Preliminary Amendment filed on 5/24/2004 under 35 U.S.C. § 132(a) as introducing new matter into the disclosure of the invention. (Office Action dated 8/14/2006, pages 4-5)

In particular, the Examiner states "[t]he amendment at page 6, paragraph 14 to "occurring in patients with sporadic glaucoma" is not supported in the specification." (Office Action dated 8/14/2006, page 4) The amendment to page 6, paragraph 14 submitted on 5/24/2004 is cancelled herein.

The amendment to insert the paragraphs after page 6, paragraph 14, submitted on 5/24/2004 has been amended according to the Examiner's suggestions. In particular, sentences 1-2, and 7-8 remain as filed. Sentences 3-6 have been deleted herein.

Applicants acknowledge that the Examiner indicated that the Specification supports the amendment at page 10, paragraph 24 filed on 5/24/2004.

The Examiner has also indicated that the Specification does not support the amendment filed on 5/24/2004 to page 28, paragraph 75. (Office Action dated 8/14/2006, page 5)

Accordingly, the present amendment cancels the amendment to page 28, paragraph 75 filed on 5/24/2004.

Claim Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1-2, 4 and 8-9 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the Specification in such a way as to reasonably convey to one skilled in relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. (Office Action dated 8/14/2006, page 6) Applicants respectfully traverse this rejection.

The Examiner contends that the claims encompass not only the alterations of the disclosed SEQ ID NO: 1, but also "include alterations in optineurin genomic sequences, which have not been taught or described by the specification". (August 14, 2006 Office Action, p. 7) Further, the Examiner contents that claims 1-2, 4 and 8-9 encompass a "large genus of nucleic acids which comprise polymorphisms in any optineurin (OPTN) gene or coding sequence which are not disclosed in the specification", while the genus is "represented in the specification by only the particularly named 4 named mutations (Table 1)". (August 14, 2006 Office Action, p. 7) The Examiner states that the disclosure fails to provide "structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations of associating an alteration or polymorphism with glaucoma". (August 14, 2006 Office Action, p. 8)

As amended, independent Claim 1 is directed to an isolated nucleic acid molecule comprising SEQ ID NO: 1, an oligonucleotide of about 10 to about 50 contiguous nucleotides of SEQ ID NO: 1, SEQ ID NO: 3, an oligonucleotide of about 10 to about 50 contiguous nucleotides of SEQ ID NO: 3, SEQ ID NO: 5, an oligonucleotide of about 10 to about 50 contiguous nucleotides of SEQ ID NO: 5, or a complement of the foregoing nucleic acid molecule, wherein the nucleic acid molecule comprises a change from GAG to AAG at codon 50, corresponding to a G to A change at position 458, and wherein the change is indicative of the presence of an optineurin-associated glaucoma or of an optineurin-associated risk of glaucoma. Independent Claim 8 is directed to an array of the nucleic acid molecules.

Claims 1 and 8 were further amended to recite a nucleic acid comprising an oligonucleotide of 10 to 50 contiguous nucleotides of SEQ ID NO: 1, SEQ ID NO: 3, or SEQ ID NO: 5, wherein the oligonucleotide comprises a change from GAG to AAG at codon 50, corresponding to a G to A change at position 458, and wherein the change is indicative of the presence of an optineurin-associated glaucoma or of an optineurin-associated risk of glaucoma. The term "contiguous" was added to clarify that a contiguous nucleotide sequence comprising the mutation is claimed. As amended, Claims 1 and 8 encompass the mutation at position 458 of the optineurin gene, which was adequately disclosed in the specification. Therefore, Claims 1 and 8 do not "encompass a large genus of nucleic acids which comprise polymorphisms in any optineurin (OPTN) gene or coding sequence". Reconsideration and withdrawal of this rejection are respectfully requested.

Claims 1-4 and 8-10 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the enablement requirement. Applicants respectfully traverse this rejection.

In making the rejection the Examiner stated:

> [W]hile being enabling for a) an isolated nucleic acid molecule comprising SEQ ID NO: 1 wherein position 458 is an A, and b) a nucleic acid molecule consisting of 10-50 contiguous nucleotide of SEQ ID NO: 1 wherein position 458 is an A, and c) the complement of either a or b, as well as an array of nucleic acid molecules attached to a solid support, the array comprising a nucleic acid molecule consisting of 10-50 contiguous nucleotide of SEQ ID NO: 1 wherein the nucleic acid molecule includes nucleotide position of SEQ ID NO: 1 and wherein the nucleotide at position 458 is an A, or complement thereof, does not provide enablement for an isolated nucleic acid molecule or an array comprising a nucleic acid molecule as set forth in the claims.

(Office Action dated 8/14/2006, page 10)

As amended, independent Claims 1 and 8 are generally directed to an isolated nucleic acid molecule comprising SEQ ID NO: 1, an oligonucleotide of about 10 to about 50 contiguous nucleotides of SEQ ID NO: 1, SEQ ID NO: 3, an oligonucleotide of about 10 to about 50 contiguous nucleotides of SEQ ID NO: 3, SEQ ID NO: 5, an oligonucleotide of about 10 to about 50 contiguous nucleotides of SEQ ID NO: 5, or a complement of the foregoing nucleic acid molecule, wherein the nucleic acid molecule comprises a change from GAG to AAG at codon

50, corresponding to a G to A change at position 458, and wherein the change is indicative of the presence of an optineurin-associated glaucoma or of an optineurin-associated risk of glaucoma.

Applicants submit that amended claims 1 and 8 overcome the foregoing rejections under 35 U.S.C. § 112, first paragraph. Claims 3 and 10 have been withdrawn. Applicants respectfully request reconsideration and withdrawal of this rejection.

Claim Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 3 and 10 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. (Office Action dated 8/14/2006, page 17) Claims 3 and 10 have been cancelled rendering this rejection moot. Applicants respectfully request withdrawal of this rejection.

Claim Rejections Under 35 U.S.C. § 102

Claims 1-4 stand rejected under 35 U.S.C. § 102(a) as being anticipated by Rezaie et al. Science, vol. 295, pages 1077-1079, (February 2002). (hereinafter "Rezaie") (Office Action dated 8/14/2006, page 18)

Applicants Tayebeh Rezaie, Anne Hawthorne Child, and Mansoor Sarfarazi are authors of the Rezaie publication. The Rezaie publication was published less than one year prior to the priority date of Claims 1-4. Pursuant to MPEP § 716.10, Applicants submit affidavits pursuant to 37 C.F.R. § 1.132 herewith, stating that the named inventors are authors of the Rezaie publication and the publication is describing the inventors' own work. The affidavits further state that co-authors Roger Hitchings, Glen Brice, Lauri Miller, Miguel Coca-Prados, Elise Heon, Theodore Krupin, Robert Ritch, Donald Kreutzer and R. Pitts Crick were working under the direction of Mansoor Sarfarazi. The inventors of the present application are Tayebeh Rezaie, Mansoor Sarfarazi and Anne Hawthorne Child

In view of the affidavits pursuant to 37 C.F.R. § 1.132, Applicants submit that the Rezaie publication cannot be used against Claims 1-2 and 4 under 35 U.S.C. 102(a). Reconsideration and withdrawal of this rejection are respectfully requested.

Claims 1-4 and 8-10 stand rejected under 35 U.S.C. 102 (a) and 102(e) as being anticipated by Fodor (U.S. Publication 2001-0053519). (Office Action dated 8/14/2006, page 18) In particular, the Examiner states "Fodor teaches an array of every possible 10 mer nucleic acid molecule. The claims encompass a genus of 10 mer nucleic acid molecules (claims 1-4) as well as an array of comprising this genus of nucleic acid molecules, which is anticipated by the teachings of Fodor." (Office Action dated 8/14/2006, page 18)

Fodor is generally directed nucleic acid sequences containing 10 or more nucleotides which can be utilized as a probe, as a primer for PCR or as a ligand. (paragraph [0003]) Fodor is further directed to nucleic probes containing 10 or more nucleotides attached to a solid support to form an array. (paragraph [0003])

To anticipate a claim, a reference must disclose each and every element of the claim. *Lewmar Marine v. Varient Inc.*, 3 U.S.P.Q.2d 1766 (Fed. Cir. 1987).

Fodor merely teaches the immensely broad genus of all 10-mer nucleic acids. Fodor does not teach any specific 10-mer, let alone teach any specific 10-mer indicative of the presence of an optineuin-associated glaucoma or an optineurin-associated risk of glaucoma. In particular, Fodor does not teach an isolated nucleic acid molecule comprising SEQ ID NO: 1, an oligonucleotide of about 10 to about 50 contiguous nucleotides of SEQ ID NO: 1, SEQ ID NO: 3, an oligonucleotide of about 10 to about 50 contiguous nucleotides of SEQ ID NO: 3, SEQ ID NO: 5, an oligonucleotide of about 10 to about 50 contiguous nucleotides of SEQ ID NO: 5, or a complement of the foregoing nucleic acid molecule, wherein the nucleic acid molecule comprises a change from GAG to AAG at codon 50, corresponding to a G to A change at position 458, and wherein the change is indicative of the presence of an optineurin-associated glaucoma or of an optineurin-associated risk of glaucoma. Thus, Fodor does not teach a mutation in the optineurin gene as required by independent Claims 1 and 8. Since Fodor does not teach every element of the claimed invention, it cannot anticipate the invention under 35 U.S.C. 102 (a) and 102(e).

In addition, new claims 44 and 45 include oligoulcleotides of 15-30 amino acids which are not taught in Fodor.

Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. 102 (a) and 102(e) rejections over Fodor.

Claims 1-4 and 8-10 stand rejected under 35 U.S.C. § 102(b), as allegedly anticipated by U.S. Patent No. 5,474,796 to Brennan. (hereinafter "Brennan") Applicants respectfully traverse this rejection. (Office Action dated 8/14/2006, pages 18-19)

Brennan is generally directed to an apparatus and methods for making arrays of functionalized binding sites on a support surface. (Abstract) Brennan also discloses a method of synthesizing every possible 10 mer oligonucleotide for use in the array. (Col. 9, ll. 49-55)

Brennan merely teaches the immensely broad genus of all 10-mer nucleic acids. Brennan does not teach any specific 10-mer, let alone teach any specific 10-mer indicative of the presence of an optineuin-associated glaucoma or an optineurin-associated risk of glaucoma. In particular, Brennan does not teach an isolated nucleic acid molecule comprising SEQ ID NO: 1, an oligonucleotide of about 10 to about 50 contiguous nucleotides of SEQ ID NO: 1, SEQ ID NO: 3, an oligonucleotide of about 10 to about 50 contiguous nucleotides of SEQ ID NO: 3, SEQ ID NO: 5, an oligonucleotide of about 10 to about 50 contiguous nucleotides of SEQ ID NO: 5, or a complement of the foregoing nucleic acid molecule, wherein the nucleic acid molecule comprises a change from GAG to AAG at codon 50, corresponding to a G to A change at position 458, and wherein the change is indicative of the presence of an optineurin-associated glaucoma or of an optineurin-associated risk of glaucoma. Thus, Brennan does not teach a mutation in the optineurin gene as required by independent Claims 1 and 8. Since Brennan does not teach element of the claimed invention, it cannot anticipate the invention under 35 U.S.C. § 102 (b). Applicants respectfully request a withdrawal of the 35 U.S.C. 102(b) rejections over Brennan and an allowance of the claims.

In addition, new claims 44 and 45 include oligoulcleotides of 15-30 amino acids which are not taught in Brennan.

Reconsideration and withdrawal of this rejection are respectfully requested.

Claims 1-2, 4, and 8-9 are rejected under 35 U.S.C. § 102 (a) as being anticipated by WO 2001/32927 to Sornasse et al. (hereinafter "Sornasse") (Office Action dated 8/14/2006, page 19) In particular, the Examiner states:

> Sornasse teaches an isolated nucleic acid molecule (SEQ ID NO: 231) which contains an alteration in at least one nucleotide sequence of SEQ ID NO: 1. One of the alterations, an insertion of a G between nucleotides 405 and 406 of

> SEQ ID NO: 1, occurs in the open reading frame of OPTN and would cause a frameshift mutation, changing most of the amino acid sequence of OPTN. This is considered to inherently indicative of the presence of OPTN associated glaucoma as it changes almost the entire OPTN amino acid sequence. Sornasse teaches microarrays comprising the nucleic acids disclosed, affixed to a solid support (see page 6).

(Office Action dated 8/14/2006, page 19)

The present invention is directed to alterations in the optineurin gene that are indicative of the presence of an optineurin-associated glaucoma or of an optineurin-associated risk of glaucoma and not directed to random mutations of the optineurin gene. Specifically, independent Claims 1 and 8 are directed to. Sornasse discloses mutations in the optineurin gene, which are not indicative of the presence of an optineurin-associated glaucoma or of an optineurin-associated risk of glaucoma, and therefore Sornasse does not anticipate the present invention. Further, Sornasse does not disclose an isolated nucleic acid molecule comprising SEQ ID NO: 1, an oligonucleotide of about 10 to about 50 contiguous nucleotides of SEQ ID NO: 1, SEQ ID NO: 3, an oligonucleotide of about 10 to about 50 contiguous nucleotides of SEQ ID NO: 3, SEQ ID NO: 5, an oligonucleotide of about 10 to about 50 contiguous nucleotides of SEQ ID NO: 5, or a complement of the foregoing nucleic acid molecule, wherein the nucleic acid molecule comprises a change from GAG to AAG at codon 50, corresponding to a G to A change at position 458, and wherein the change is indicative of the presence of an optineurin-associated glaucoma or of an optineurin-associated risk of glaucoma. For this reason, at least, Sornasse does not teach all of the elements of invention and therefore does not anticipate Claims 1-2, 4 and 8-9.

Applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. § 102 (a) rejections over Sornasse .

Claim Rejections Under 35 U.S.C. § 103(a)

Claims 8-10 stand rejected under 35 U.S.C. § 103(a), as allegedly unpatentable over Rezaie in view of Fodor and Brennan. (Office Action dated 8/14/2006, pages 19-20) Applicants respectfully traverse this rejection.

For an obviousness rejection to be proper, the Examiner must meet the burden of establishing a *prima facie* case of obviousness, i.e., that all elements of the invention are

disclosed in the prior art; that the prior art relied upon, coupled with knowledge generally available in the art at the time of the invention, contain some suggestion or incentive that would have motivated the skilled artisan to modify a reference or combined references; and that the proposed modification of the prior art had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *In re Fine*, 5 U.S.P.Q.2d 1596, 1598 (Fed. Cir. 1988); *In Re Wilson*, 165 U.S.P.Q. 494, 496 (C.C.P.A. 1970); *Amgen v. Chugai Pharmaceuticals Co.*, 927 U.S.P.Q.2d, 1016, 1023 (Fed. Cir. 1996).

Rezaie discloses the causative gene of dominantly inherited adult-onset POAG on chromosome 10p14, designated OPTN. (Abstract) Rezaie further discloses mutations in the OPTN gene, including a change GAG to AAG at codon 50 which is a POAG mutation in OPTN. (Fig. 1) Rezaie teaches screening glaucoma case for changes in the OPTN sequence using single-strand polymorphism (SSCP) analysis. (page 1078, Col. 3) As noted by the Examiner, Rezaie does not teach an array of nucleic acids attached to a solid support comprising a nucleic acid used detect or sequence optineurin polynucleotides by hybridization comprising 10-50 contiguous nucleotides of SEQ ID NO: 1.

Fodor and Brennan are cited by the Examiner for teaching methods of detecting nucleic acid targets using nucleic acid probes attached to a solid support. In particular, Fodor and Brennan teach arrays comprising a plurality of nucleic acid sequences suitable for gene expression analysis or for oligonucleotides that bind to biologically active macromolecules, respectively.

Neither Fodor or Brennan make up for the deficiency of Rezaie. Neither Fodor nor Brennan teach the use of arrays to detect single amino acid changes in a gene associated with a specific disease or disorder. Specifically, neither, Fodor or Brennan teach an array of nucleic acids attached to a solid support comprising an isolated nucleic acid molecule comprising SEQ ID NO: 1, an oligonucleotide of about 10 to about 50 contiguous nucleotides of SEQ ID NO: 1, SEQ ID NO: 3, an oligonucleotide of about 10 to about 50 contiguous nucleotides of SEQ ID NO: 3, SEQ ID NO: 5, an oligonucleotide of about 10 to about 50 contiguous nucleotides of SEQ ID NO: 5, or a complement of the foregoing nucleic acid molecule, wherein the nucleic acid molecule comprises a change from GAG to AAG at codon 50, corresponding to a G to A change at position 458, and wherein the change is indicative of the presence of an optineurin-associated

glaucoma or of an optineurin-associated risk of glaucoma.. Thus, in summary, since the combination of Rezaie in view of Fodor and Brennan does not teach all the elements of independent Claim 8, Applicants believe that the Examiner has not made a *prima facie* case of obviousness. Applicants respectfully request a withdrawal of the § 103 rejection of Claims 8 and 9 over Rezaie in view of Fodor and Brennan. Claim 10 has been withdrawn rendering the rejection of this claim moot.

It is believed that the foregoing amendments and remarks fully comply with the Office Action and that the claims herein should now be allowable to Applicants. Accordingly, reconsideration and withdrawal of the objection(s) and rejection(s) and allowance of the case are respectfully requested.

If there are any additional charges with respect to this Amendment or otherwise, please charge them to Deposit Account No. 06-1130.

Respectfully submitted,

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